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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,425	05/30/2007	Tomoko Ono	2352.014	1952

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
10/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,425	ONO ET AL.	
	Examiner	Art Unit	
	GAILENE R. GABEL	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/22/06; 9/26/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendment

1. Applicant's preliminary amendment filed June 22, 2006, is acknowledged and has been entered. Claims 1, 4, and 5 have been amended. Currently, claims 1-6 are pending and are under examination.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

3. Figure 1 is objected to under 37 CFR 1.83(a) because it fails to show units that define the X and Y axes of the graph. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate

changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

4. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(I) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Information Disclosure Statement

5. The listing of references in the specification at pages 3-4 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. In this case, it is unclear what essential structural and functional cooperative relationships exist between "von Willebrand factor cleaving protease" or "vFW-cleaving protease" and either one of

thrombosis and degree of thrombophilia. Does a decrease of vWF-cleaving protease provide indication of thrombosis? Does a decrease or increase of vWF-cleaving protease provide degree of thrombophilia? Please clarify.

Claim 1 is also indefinite in being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In this case, a correlation step which correlates a measured value of vWF-cleaving protease and thrombosis or degree of thrombophilia is missing. For example, does a decreased level of vWF-cleaving protease correlate directly to the occurrence of thrombosis or degree of thrombophilia? Does any amount of decrease in value of vWF-cleaving protease provide indication of the occurrence of thrombosis or degree of thrombophilia?

Claim 1 is vague and indefinite in reciting, "A method of detecting... and measuring a von Willebrand factor-cleaving protease" because it is unclear as recited as to whether the claimed method is qualitative diagnostic method or a quantitative diagnostic method. It is specifically unclear as to whether a decrease or increase in vWFcp is detected or the amount of vWFcp is quantitated, and how the result correlates to thrombosis or degree of thrombophilia.

Claim 1 is also ambiguous because it is unclear how thrombosis and degree of thrombophilia which are different diseases or conditions, can be differentially detected and determined as claimed. See also claim 3.

Claim 1 is ambiguous in reciting, "measuring a von Willebrand factor-cleaving protease" because it fails to clearly define the source of the analyte, i.e. type of sample, as well as the test subject.

Claim 2 is confusing in reciting, "thrombosis is selected from the group consisting of acute or chronic myeloid leukemia…., systemic lupus erythematosis (SLE)…, cerebral infarction…" because it is unclear how thrombosis is leukemia, SLE, or infarction etc. The listed diseases do not appear to be characterized as "thrombosis." How is leukemia or SLE thrombosis. Does Applicant perhaps intend that thrombosis is manifested in these diseases? Please clarify.

Claim 4 provides for the use of "decreased concentration of the vWF-cleaving protease as an index in comparison to healthy people", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 4 is indefinite in reciting "decreased concentration" because "decreased" is a relative term that lacks a comparative basis for defining its metes and bounds. How decreased or low is the concentration of vWFcp in comparison to normal healthy control, so as to be an index or marker of thrombosis or degree of thrombophilia.

Claim 4 is also indefinite in reciting, "healthy people" because the term "healthy" is a subjective term that lacks a comparative basis for defining its metes and bounds.

Claim 6 is indefinite in reciting, "A kit … characterized by comprising…" because it is unclear what Applicant intends to encompass in reciting, "characterized" as used in the claim. Does Applicant simply intend, "A kit … comprising…"?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Konetschny et al. (Development of a Highly Sensitive and Specific Enzyme-linked Immunosorbent Assay for the Detection of ADAMTS-13 in Human Plasma, Blood 102 (11) Abstract #4062 (November 16, 2003)).

Konetschny et al. teach that von Willebrand factor (vWF) predominantly released from endothelial cells, when stimulated, are released as high molecular weight multimeric proteins having a large portion of unusually large vWF (ULVWF) which is hemostatically very active in efficiently interacting with platelet receptors and very effective in promoting platelet adhesion to sites of vascular injury. However, prolonged presence of hyperactive ULVWF leads to platelet aggregation and thrombus formation leading to thrombosis such as thrombotic thrombocytopenic purpura (TTP). Konetschny et al. teach a method of detecting occurrence of thrombosis in human plasma sample by measuring the amount of von Willebrand factor-cleaving protease (vWFcp) present in

the sample using highly sensitive and specific enzyme-linked immunosorbent assay (ELISA). vWFcp (ADAMTS-13) is a metalloprotease discovered to actively regulate proteolytic degradation of ULVWF and that severe deficiency in vWFcp is also observed in acquired and hereditary TTP (1st full paragraph). In practice, Konetschny et al. teach immunologically measuring the amount of vWFcp that bound to the antibody by combining a blood sample from the patient with antibodies (anti-vWFcp) that specifically bind to vWFcp. Capture anti-vWFcp (anti-ADAMTS-13) polyclonal antibody is coated onto microtiter plate to capture vWFcp and detection anti-vWFcp MAb (242/H2) is conjugated to alkaline phosphatase so as to provide binding, detection, and measurement of vWFcp antigen present in the plasma (2nd full paragraph). Konetschny et al. show that a decrease in concentration of vWFcp (deficiency in ADAMTS-13) in a patient in comparison to healthy control provides indication of occurrence of thrombosis (1st and 3rd full paragraphs).

8. Claims 1, 2, and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Scheiflinger et al. (US 2004/0214346 A1).

Scheiflinger et al. disclose a kit and diagnostic method for detecting and determining diagnosis of thrombosis manifested in a patient blood sample (plasma) by measuring the amount of vWFcp in the plasma sample [0015, 0029, 0032]. Thrombosis may be manifested in the form thrombotic microangiopathy or TM, hemolytic uremic syndrome (HUS), systemic lupus erythematosis (SLE), and cancer-associated TM [0034]. In practice, Scheiflinger et al. teach combining a blood sample from the patient

with anti-vWFcp antibody that specifically binds to vWFcp immobilized into a solid phase and then detecting binding and complex formation of the anti-vWFcp antibody to vWFcp antigen using the immunological assay kit and method. The amount of vWFcp that bound to the anti-vWF antibody is also measured [0032]. Scheiflinger et al. show that a decrease in concentration of vWFcp in a patient in comparison to healthy control provides indication of occurrence of thrombosis ([0055, 0056]; Table 3).

9. Claims 1, 2, and 4-6 are rejected under 35 U.S.C. 102(a) as being anticipated by Soejima et al. (EP 1 544 293).

Soejima et al. teach an antibody showing immunoreactivity selectively to vWFcp (ADAMTS-13). The antibody is specifically used to purify and detect vWFcp antigen, as well as diagnosis and treatment of thrombosis such as TTP (Abstract; [0008, 0018, 0047]). Soejima et al. provide that high molecular weight multimeric proteins having a large portion of ULVWF play significant roles in promoting platelet aggregation and microthrombus formation under high shear stress. Soejima et al. also provide that vWF and ULVWF are decomposed at the position 842Tyr-843Met by vWFcp antigen in circulating blood of healthy people under high shear stress [0004]. Soejima et al. specifically teach monoclonal antibodies which specifically bind vWFcp. The monoclonal antibodies include WH10, WH2-22-1A, and WH63.1 [2;12]. These monoclonal antibodies may be individually incorporated into a kit format [19, 0052]. Soejima et al. teach detecting or determining occurrence of thrombosis in a patient blood sample (plasma) by immunologically measuring the amount of vWFcp present in

the sample using the vWFcp MAbs in ELISA or radioimmunoassay (RIA) [25, 26, 0040, 0042, 0047]. Soejima et al. show that a decrease in concentration of vWFcp in the patient in comparison to healthy control provides indication of occurrence of thrombosis ([0049, 0083] and Table 3). Additionally, the monoclonal antibody may be formulated into a pharmaceutical composition for administration of effective amount of the antibody to treat thrombosis such as TTP [0061].

10. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Igami et al. (US 2009/0220990).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Igami et al. teach a kit and method for detecting thrombosis and/or determining degree of thrombophilia in a patient blood sample (plasma) by measuring the amount of vWFcp (ADAMTS-13) present in the sample [0045, 0047, 0053-0055]. According to Igami et al., a plasma blood sample from the patient is contacted with antibody that specifically binds to vWFcp. The sample mixture is then detected for the binding of the anti-vWFcp antibody to the vWFcp antigen present in the sample and immunologically measured for the amount of vWFcp that is present in the sample [0015, 0017, 0040]. Igami et al. provide that a decrease in concentration of vWFcp in the patient in comparison to healthy control subjects not exhibiting thrombosis or thrombophilia provides indication of occurrence of thrombosis (atherothrombotic cerebral infarction)

and/or degree of thrombophilia [0007, 0033, 0036]. Thrombosis is taught by Igami et al. to be associated with cerebral infarction such as cerebral thrombosis, acute or chronic myeloid leukemia (AML or CML), acute promyelocytic leukemia, SLE, pulmonary embolism, veno-occlusive disease, acute lymphocytic leukemia (ALL), TM, TTP, HUS, and deep vein thrombosis leukemia [0004, 0005, 0008].

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

September 29, 2009